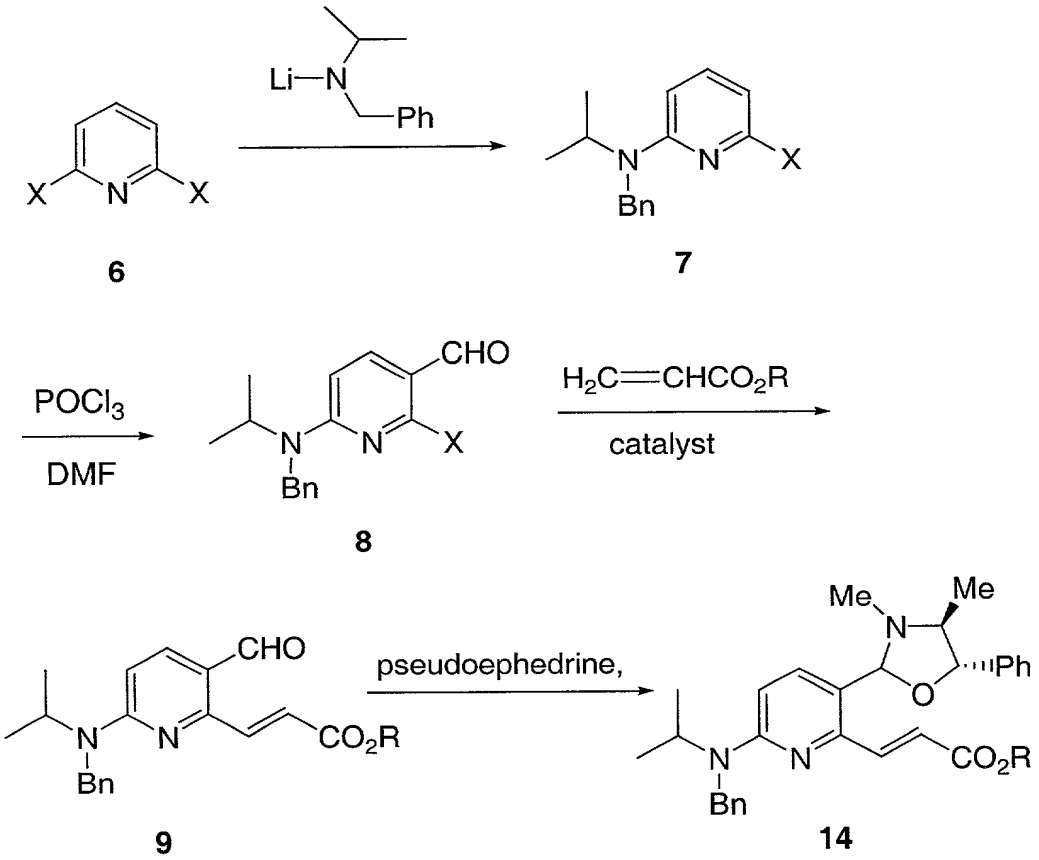
from the group consisting of aryl, CO_2R^4, CF_3, $N(R^5)2$, $(C_1$-$C_8)$-alkoxy, $(C_1$-$C_8)$-alkyl, $(C_2$-$C_8)$-alkenyl, $(C_2$-$C_8)$alkynyl, $(C_3$-$C_8)$cycloalkyl, $CO(CH_2)_nCH_3$, and $CO(CH_2)_nCH_2N(R^5)_2$; and n is 0 to 5.

Reaction Scheme B below shows a method for the preparation of α, β-unsaturated ester involving an amination, a formylation and a Heck reaction.

REACTION SCHEME B



X = halo; R = $(C_1$-$C_6)$-alkyl

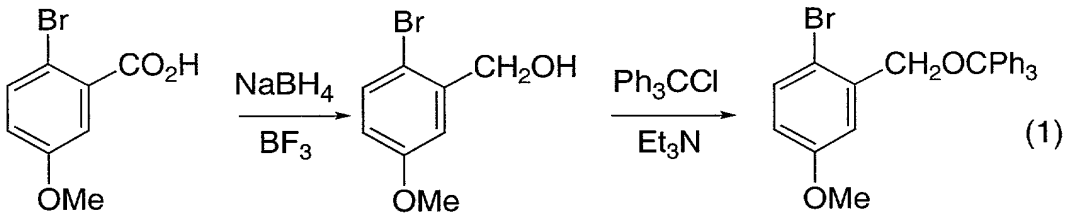
Commercially available disubstituted pyridine (6) is aminated by lithium N-isopropylbenzylamide to afford the compound (7). The aminated compound (7) was then regiospecifically formylated to give aldehyde compound (8) upon treatment with about 4 equivalents of $POCl_3$ in dimethylformamide (DMF) at a temperature range of about 35°C to about 70°C. The aldehyde compound (8) then undergoes a Heck

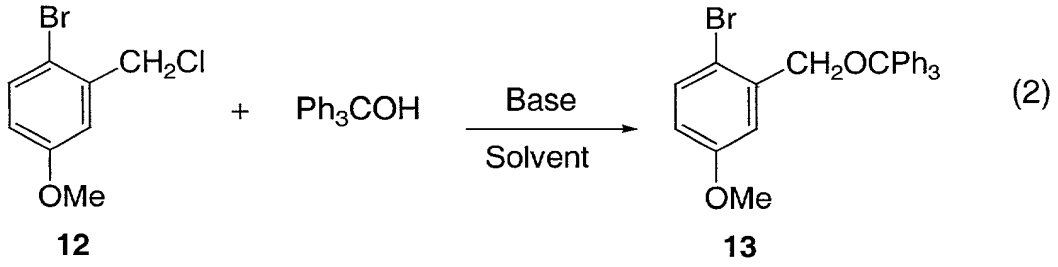
reaction with 1 to 5 equivalents of (C_1-C_6)-alkyl acrylate in the presence of an aprotic solvent, a base and a catalyst at a temperature range of 80°C and 110°C to provide the unsaturated ester (9) in high yield. The unsaturated ester (9) is then reacted with a chiral additive such as pseudoephedrine or N-methyl-cis-aminoindanol (not shown in the scheme) to give the protected aldehyde (16).

The aprotic solvent for a Heck reaction is selected from dimethylacetamide (DMAC), dimethylformamide (DMF), toluene and acetonitrile, and a base is selected from CH_3COONa, $CH_3COONa{\bullet}3H_2O$ and $NaHCO_3$. Preferred solvent and base are DMAC and $CH_3COONa{\bullet}3H_2O$, respectively. Water may be added (about 6 equivalents) to the reaction mixture to enhance the reaction rate. For example, the reaction rate in the presence of CH_3COONa with water is 6 hours, whereas the reaction without water is 20 hours. The catalyst for the reaction is selected from $PdCl_2(dppf)_2$, $PdCl_2(PPh_3)_2$, $Pd(dba)_2$, $PdBr_2$, $Pd(OAc)_2$, and $(allyl)_2PdCl_2$ dimer with tri-o-tolylphosphine. Preferred catalyst is $PdCl_2(dppf)_2$.

Another aspect of the invention involves the synthesis of a bottom piece (13), ArX (X is halo), of the compound according to Reaction Scheme C.

REACTION SCHEME C





In Reaction Scheme C, the bottom piece of 2-Bromo-5-methoxybenzyl trityl ether (13) can be prepared either by a route (1) or a route (2). The route (1) involves a two-step

synthesis via a reduction and a protection, whereas the route (2) provides a one-step synthesis by using commercially available benzyl chloride (12) in the presence of a base and an aprotic solvent. The base is selected from potassium tert-butoxide, KOH or NaH, and the solvent is selected from DMAC, DMSO or DMG. A mixture of potassium *tert*-butoxide and dimethyl acetamide (DMAC) is preferred. The compound (13) can be readily isolated by addition of water. As shown in Table 2 below, the optimal charge ratio of benzyl chloride (12):Ph_3COH:*tert*-BuOK is 1:1.1:1.05 with slow addition of the benzyl chloride.

Table 2. Preparation of 2-bromo-5-methoxybenzyl trityl ether (13)

Entry	Ph_3COH (eq)	**12** (eq)	t-BuOK (eq)	Addition of **12**	Yield, **13** (% yield)
1	1.1	1.0	1.05	1h	87%
2[a]	1.1	1.0	1.05	1h	82%
3	1.0	1.05	1.0	1h	82%
4	1.1	1.0	1.05	5 min	79%

[a]1% water is added to DMAC